SYNOPSIS OF THE THESIS

ORGANO SULPHUR AND SELENIUM COMPOUNDS

("Synthesis, Characterization, and Biological Evaluation of some(E)- and (Z)- sulphides, sulphones, sulphide-sulphones, di sulphones and some related selenium containing compounds")

Submitted to

SRI KRISHNADEVARAYA UNIVERSITY

ANANTAPUR -515 055, A.P., INDIA

By

N. PENCHALAIAH **M.Sc.,**

Under the Research supervision of

Prof. G. NARAYANA SWAMY

Department of Chemistry

In partial fulfillment for the award of the degree of

DOCTOR OF PHILOSOPHY

IN

CHEMISTRY

July-2012

ORGANO SULPHUR AND SELENIUM COMPOUNDS

("Synthesis, Characterization, and Biological Evaluation of some(E)- and (Z)- sulphides, sulphones, sulphide-sulphones, di sulphones and some related selenium containing compounds ")

Elemental Sulphur and Selenium have a long history of application in medicine as a result of scabicidal, insecticidal, fungicidal and purgative properties. A large number of organosulphur and selenium compounds are known to posses chemotherapeutic activity and great potency as drugs. The chemical versatility of organosulphur and selenium compounds has lead to their incorporation into a number of projects in several different areas of medicinal chemistry. The discovery of sulphonamide as antibacterial drug by a German scientist, Gerhard Domgak, marks an important milestone in the development of medicinal chemistry. This discovery leads to the synthesis of some 15,000 sulphonamides. A wide variety of organosulphur compounds show useful biological activity. They have become a regular armoury of pharmaceutical and crop protection chemistry. The antibiotics like penicillin, ampicillin, amoxycillin are organosulphur compounds. Anti-ulcer drugs ranitidine and cematidine which are thioethers (organosulphide), and pentaprazole, omeprazole, lansoprazole and rabeprazole which are organosulphones are extremely effective and in many cases their use can avoid the need of surgery in the treatment of ulcer. Of the current agrochemicals some 30% contain sulphur in wide variety of oxidation states, because of their useful biological activity.

The element Selenium is exceedly effective in the prevention of necrotic liver degeneration. The element has been shown to be constantly present in the tissues of higher animals. It is one of the most essential elements in human being.

Selenium compounds can act as antiparasitic agents, analgesics, local anaesthetics, anti inflammatory compounds, anti histamines and anti cancer agents. Some times selenium analogues behave as potential as sulphur analogues and some times more active than sulphur analogues.

Organosulphur compounds include organosulphides (thioethers), sulphoxides and sulphones etc. Of these, the synthesis and structural studies of simple sulphides, sulphones and sulphoxides are well known thing for a long time, but the studies on 1,1-bis(alkyl- or arylthio)ethylenes and their corresponding bis-sulphones and 1,2- bis(alkyl- or arylthio)ethylenes and their corresponding bis-sulphones are of recent origin. The biological studies on sulphones revealed that they can be used in chemotherapy and agriculture. The sulphones of chlorothiazide and hydrochlorothiazide series are frequently used as diuretics. Sulphonal, $(CH_3)_2C(SO_2C_2H_5)_2$, trional and tetranal are used as sedatives and hypnotics. The discovery of dapsone as potential drug against leprosy has revolutionized its whole treatment. Dapsone is also proved to be a potent prophylactic agent.

The recently originated unsaturated disulphones revealed from their biological studies that they can be used as effective fungicides. A few mercapto haloethylene sulphone derivatives, bis(organosulphonyl)ethylenes with the general formula $R_1SO_2(R_2)C=C(R_3)SO_2R_4$, vinylene sulphonyl compounds and bis(arylthio)ethylenes have been reported as effective fungicides to protect seed. They are also effective against mildew on cotton-cloth, paint and various plant foliage diseases. The activity of organosulphur compounds of biological importance as been found to vary depending

upon the substituents present and also on the stereochemical configurations of the substances.

When the present work was undertaken, only a very few number of unsaturated sulphide-sulphones, disulphones, selenylsulphides and selenonylsulphones were known and the physico-chemical data available in the geometrical isomers of these compounds is also scanty. With these considerations the author undertook the synthesis of some new (*E*) - and (*Z*)-unsaturated sulphides, sulphones, sulphide-sulphone, disulphones selenylsulphides and selenonylsulphones to establish their geometrical configurations by stereo specific synthesis and spectral (IR, NMR, and Mass) studies.

In1963 Benati and his co-workers reported the preparation of cis- and trans- 1,2-bis(p-bromophenylsulphonyl)stilbenes. Truce and his co-workers reported the preparation of 1, 2-bis (alkylthio) ethylenes by the nucleophilic displacement of halogens with thiols from tetrachloroethylene, dichloroethylene, vinyledine halides and vinyl halides. Another important method of preparing these compounds is by the addition of thiols to acetylenes.

The entire work of the thesis entitled **"Synthesis, characterization, and Biological Evaluation of some newer sulphur, selenium containing compounds"** is divided into **5 chapters.**

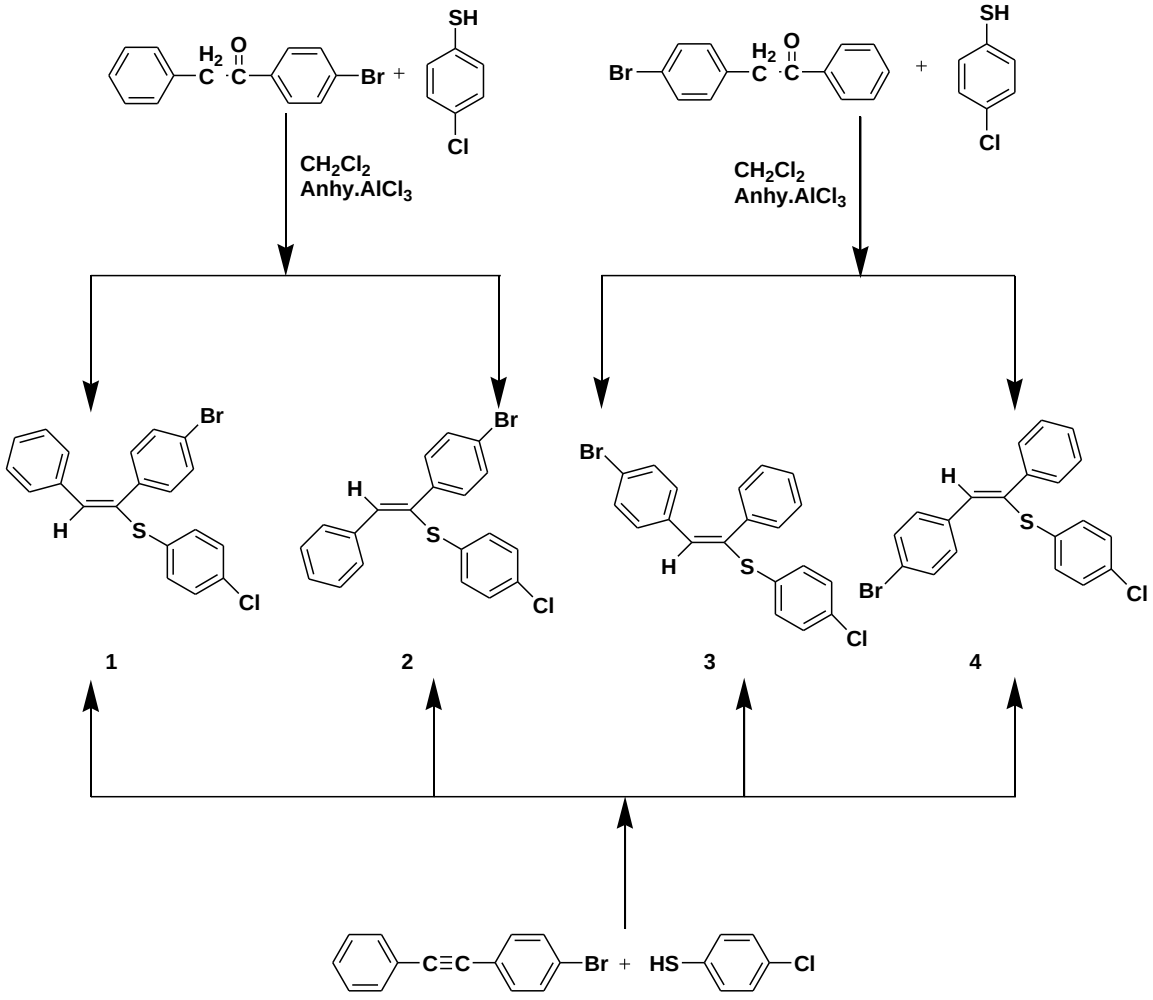
Chapter 1 summarizes the historical overview on unsaturated sulphides, sulphones, sulphide-sulphones, di sulphones, selenylsulphides,selenonylsulphones.

Chapter 2 deals with the preparation of starting materials like benzyl *p*-bromophenyl ketone, *p*-bromobenzyl phenyl ketone and *p*-bromophenyl phenyl acetylene by known procedures. In the present investigation two pairs of monosulphides, monosulphones, bromosulphides, bromosulphones, sulphide-sulphones, a pair of disulphones, two pairs of

selenylsulphides and selenonylsulphones have been synthesized according to the schemes **1, 2 , 3 , 4** and **5.** The synthesis of these compounds is also confirmed starting from acetylene. The thiols *(p*-chloro thiophenol) and phenyl selenyl bromide required for the work has been obtained from commercial source.

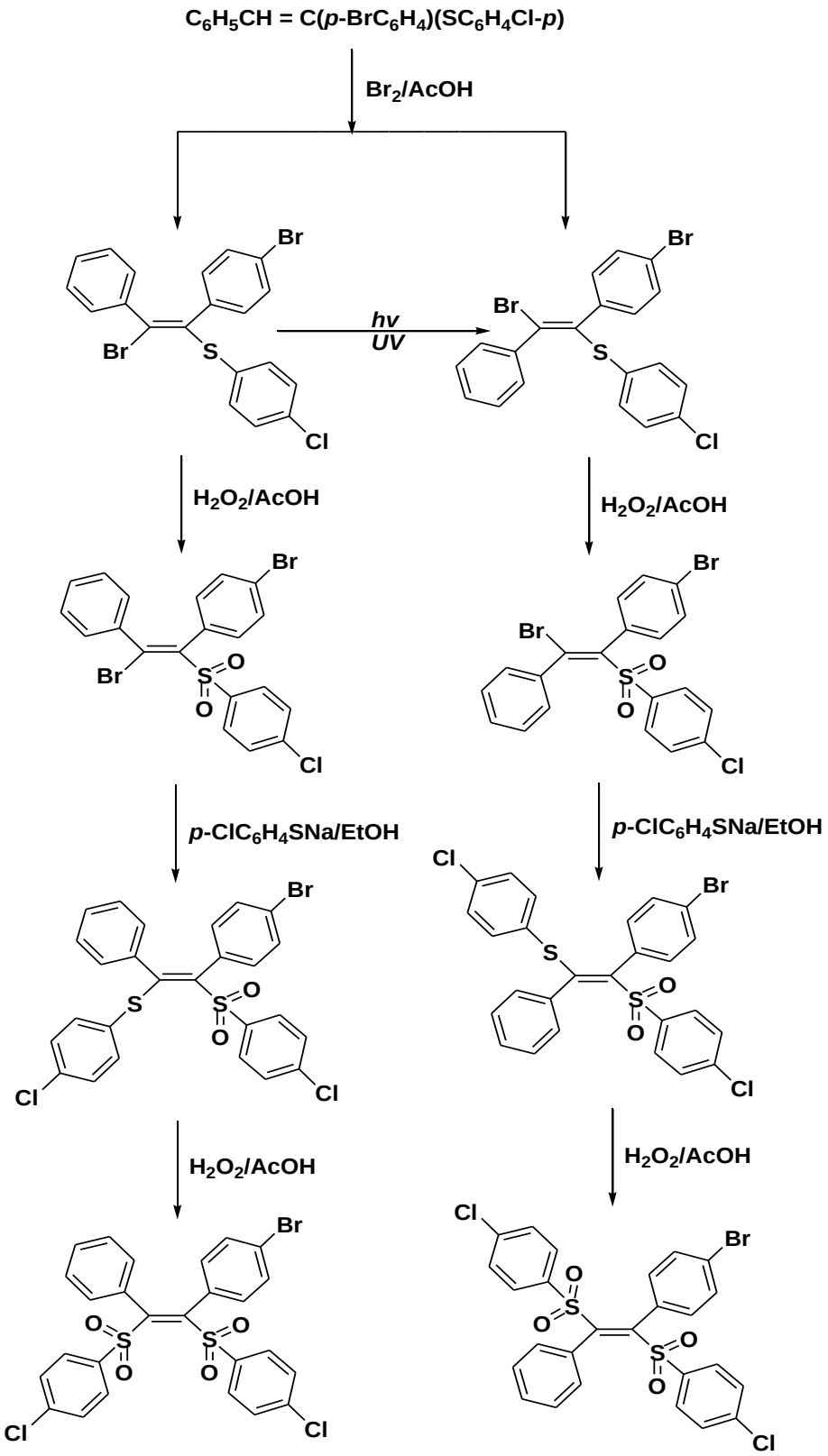
REACTION SCHEMES:

Method 1

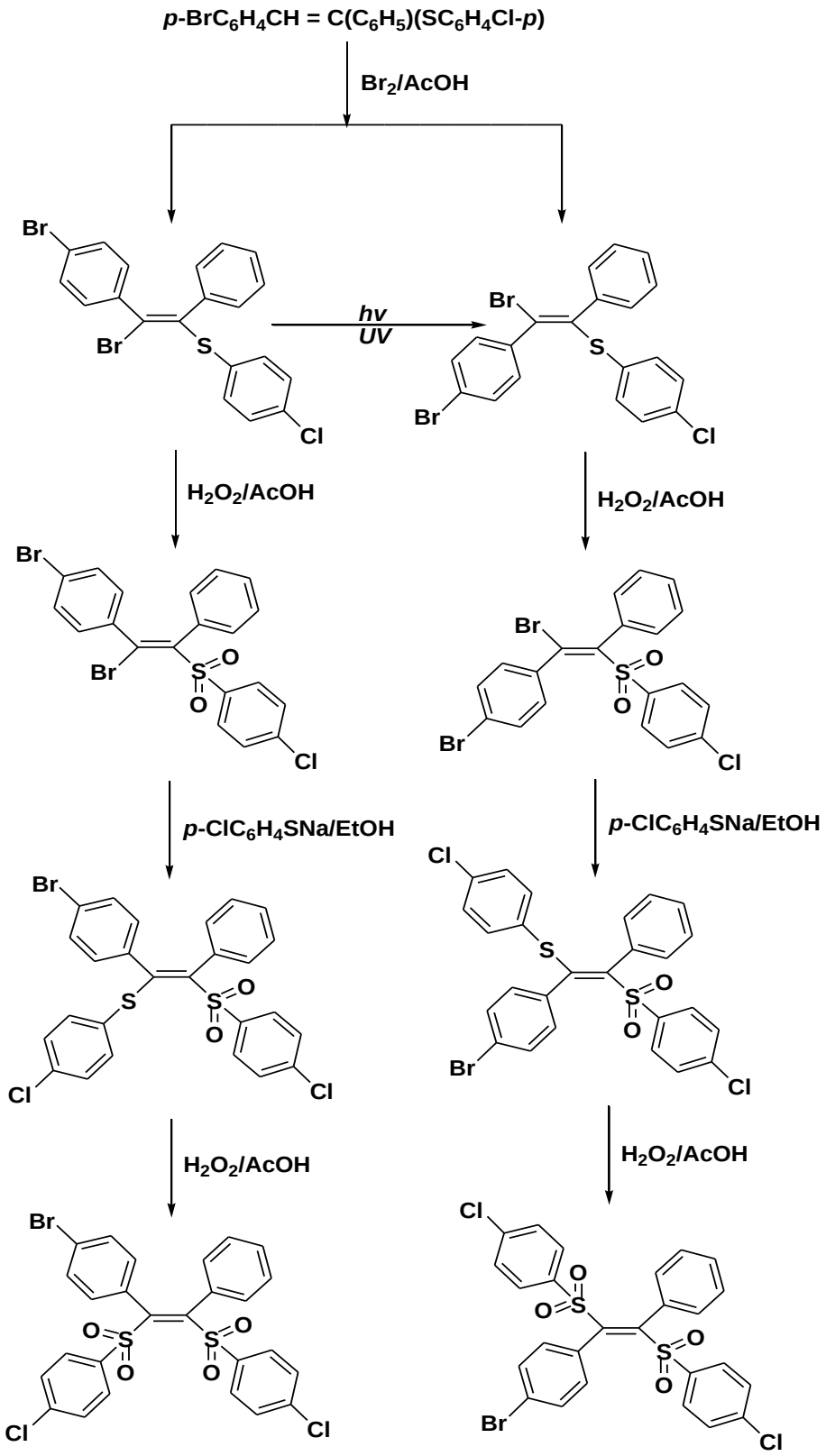


Method 2

Scheme-1

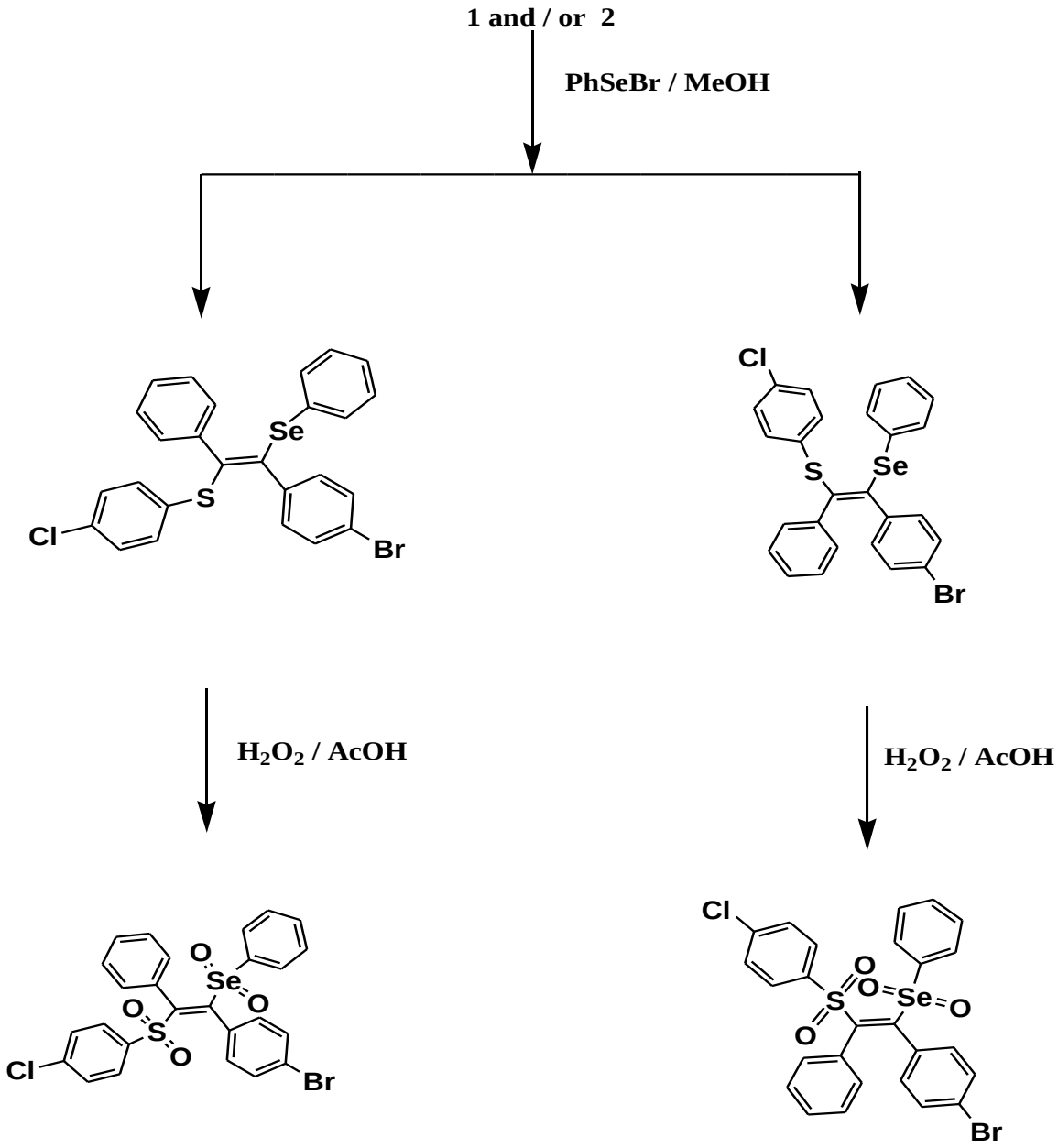

C6H5CH = C(p-BrC6H4)(SC6H4Cl-p)
Br2/AcOH
hv
UV
H2O2/AcOH
H2O2/AcOH
p-ClC6H4SNa/EtOH
p-ClC6H4SNa/EtOH
H2O2/AcOH
H2O2/AcOH
Br
Cl
S
O

Scheme -2.

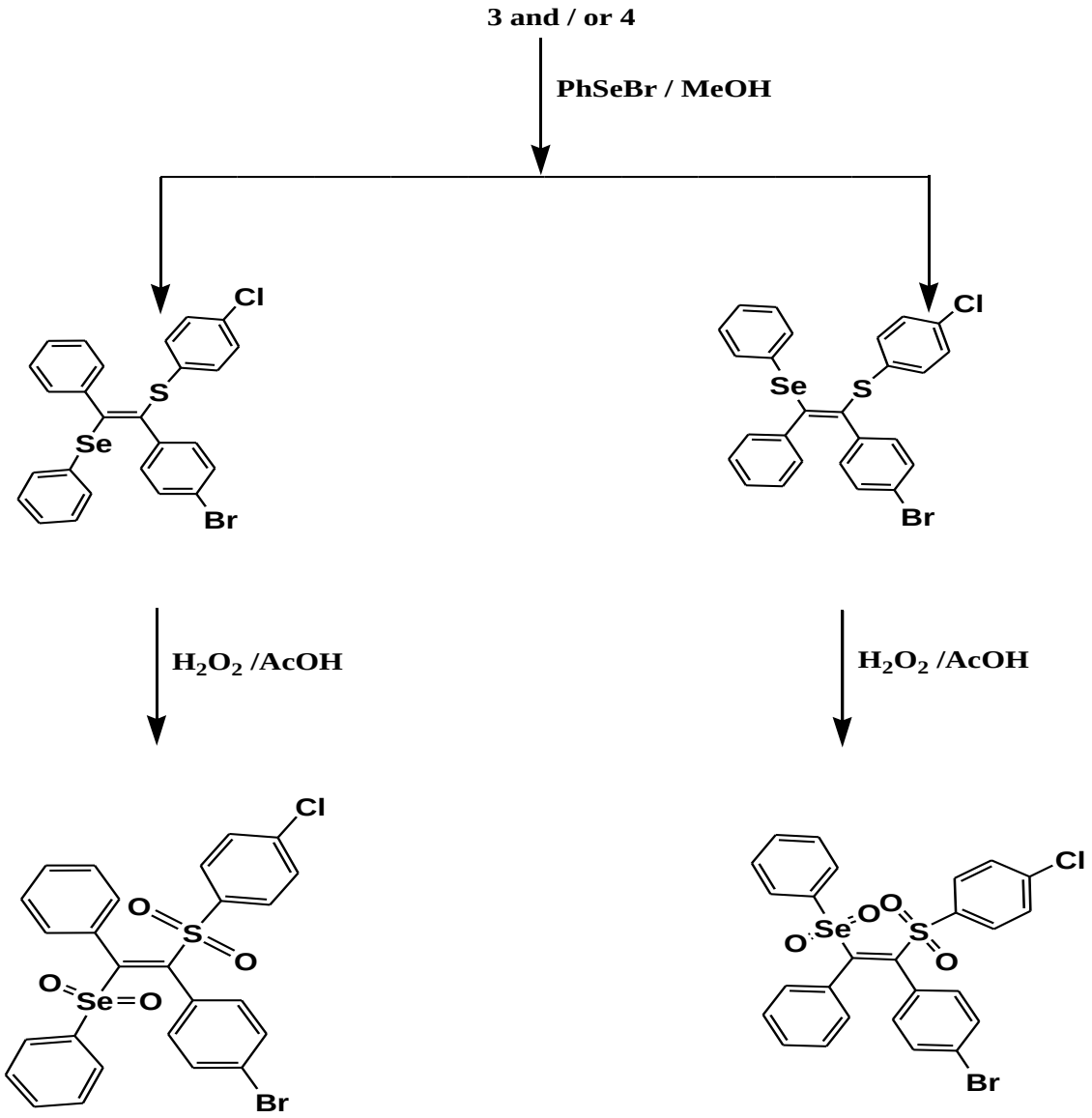

p-BrC6H4CH = C(C6H5)(SC6H4Cl-p)
Br2/AcOH
hv
UV
H2O2/AcOH
H2O2/AcOH
p-ClC6H4SNa/EtOH
p-ClC6H4SNa/EtOH
H2O2/AcOH
H2O2/AcOH

Scheme -3.

(*E*)-1,2-bis (*p*-chloro phenyl sulphonyl)-1-*p*-bromophenyl-2-phenylethylene has been prepared by two different methods and these stereospecific methods of synthesis confirmed that it is a *trans* isomer. (*Z*)- 1,2-bis (*p*-chloro phenyl sulphonyl)-1-*p*-bromo phenyl- 2- phenyl ethylene has been prepared by two different methods and these stereo specific methods of synthesis confirmed it to be a *cis*-isomer.



Scheme -4.



Scheme -5.

About 2 pairs of monosulphides, 2 pairs of monosulphones, 2 pairs of bromosulphides, 2 pairs of bromosulphones, 2 pairs of sulphide-sulphones, a pair of bis sulphones, 2 pairs of selenylsulphides, 2 pairs of selenonylsulphones have been synthesized according to the schemes shown above.

Chapter 3 deals with the characterization of all the above synthesized compounds by IR, ^{1}H NMR and Mass spectroscopic methods.

Chapter 4 deals with the screening of all the above synthesized compounds for their biological activity (antibacterial and antifungal activity) using five bacteria and two fungi. It was observed that the antimicrobial activity was good for some of the compounds.

Chapter 5 describes the summary of experimental results incorporated in the thesis.

LIST OF RESEARCH PUBLICATIONS:

1. Scholars Research Library, Der Pharma Chemica, 2012, 4 (2): 613-621

Synthesis and Antifungal activity of Novel unsaturated Diastereomeric (*E* and *Z*) Sulphur derivatives

N. Penchalaiah, R. Mallikarjuna Rao, L. Vinay Kumar, P. Jagan Naik, A. Babul Reddy and G. Narayana Swamy*

Department of Chemistry, Sri Krishnadevaraya University, Anantapur, Andhra Pradesh, India.

2. Journal of Chemical and Pharmaceutical Research, 2012, 4(3): 1523-1531

Synthesis and antibacterial activity of novel unsaturated diastereomeric (*E* and *Z*) sulphur compounds

N. Penchalaiah, R. MallikarjunaRao, L. Vinay Kumar, P. Jagan Naik, A. Babul Reddy, and G. Narayana Swamy*

Department of Chemistry, Sri Krishnadevaraya University, Anantapur, Andhra Pradesh, India.

3. Scholars Research Library, Der Pharma Chemica, 2012, 4(2): 674-678

Synthesis, characterization of some derivatives of 3-[(4-chlorophenyl) sulphonyl] propane hydrazide.

L.Vinay Kumar, P. Jagan Naik,T.ChandraSekhar, **N.Penchalaiah,** A.BabulReddy and G. Narayana Swamy*

Department of Chemistry, Sri Krishnadevaraya University, Anantapur, Andhra Pradesh, India.

4. *Phosphorus, Sulfur, and Silicon*, 186:1721–1732, 2011

Synthesis and Biological Evaluation of Diastereomeric (E and Z) Sulfides, Sulfones, Sulfide-Sulfones, and Disulfones

A. Babul Reddy [a,] A. Hymavathi [a,] L. Vinay Kumar [a,] **N.Penchalaiah** [a,] & G. Narayana Swamy* [a]

[a,] *Department of Chemistry, Sri Krishnadevaraya University, Anantapur, Andhra Pradesh, India.*

5. Scholars Research Library, Der Pharma Chemica, 2010, 2(5): 438-445

Stereo selective synthesis and antimicrobial activity of congested Epoxysulphones

A Babul Reddy, A. Hymavathi, L. Vinay Kumar, **N. Penchalaiah,** and G. Narayana Swamy*

Department of Chemistry, Sri Krishnadevaraya University, Anantapur, Andhra Pradesh, India.

6. Journal of Chemical and Pharmaceutical Research (Volume-3 issue- 4 Oct - Dec'2010: 267-269)

Synthesis, characterization and microbial evaluation of unsaturated Selenium compounds

JaganNaik P., VinayKumar L., BabulReddy A., Karunasree M., **Penchalaiah N.**, and G. Narayana Swamy*

Department of Chemistry, Sri Krishnadevaraya University, Anantapur, Andhra Pradesh, India.

7. Journal of Chemical and Pharmaceutical Research volume-2 issue-4 October-December, 2009:253-255

Synthesis,characterization and biological activities of some sulphides and sulphones from chalcones

Vinay Kumar Lakkakula, Jagan Naik Pujari, **Penchalaiah Nali,** and Narayana Swamy Golla*

Department of Chemistry, Sri Krishnadevaraya University, Anantapur, Andhra Pradesh, India.